

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims

Sub C1
1. (Previously Twice amended) A method for the treatment of cancerous cell growth mediated by RAF kinase, comprising administering a compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is $-\text{NH}-\text{C}(\text{O})-\text{NH}-$,

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A is a substituted moiety of up to 40 carbon atoms of the formula: $-\text{L}-(\text{M}-\text{L}^1)_q$, where L is a 5 or 6 membered cyclic structure bound directly to D, L^1 comprises a substituted cyclic moiety having at least 5 members, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and L^1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur,

wherein L^1 is substituted by at least one substituent selected from the group consisting of $-\text{SO}_2\text{R}_x$, $-\text{C}(\text{O})\text{R}_x$ and $-\text{C}(\text{NR}_y)\text{R}_z$,

R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo,

R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms

selected from N, S and O and are optionally substituted by halogen;

R_x is R_z or NR_aR_b where R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

$-OSi(R_f)_3$ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R_a or R_b is $-C(O)-$, a C_1-C_5 divalent alkylene group or a substituted C_1-C_5 divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_1-C_5 divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L^1 is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and W_n , where n is 0-3;

wherein each W is independently selected from the group consisting of $-CN$, $-CO_2R^7$, $-C(O)NR^7R^7$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, $-Q-Ar$, and

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carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NR⁷R⁷, -NO₂, -NR⁷C(O)R⁷, -NR⁷C(O)OR⁷ and halogen up to per-halo; with each R⁷ independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m- CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, and X^a is halogen; and

B2 cont
Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of -CN, -CO₂R⁷, -COR⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NO₂, -NR⁷R⁷, -NR⁷C(O)R⁷, and -NR⁷C(O)OR⁷, with R⁷ as defined above.

2. (Previously Twice amended) A method as in claim 1 wherein:

R_y is hydrogen, C₁₋₁₀ alkyl, C₁₋₁₀ alkoxy, C₃₋₁₀ cycloalkyl having 0-3 heteroatoms, C₂₋₁₀ alkenyl, C₁₋₁₀ alkenoyl, C₆₋₁₂ aryl, C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from N, S and O, C₇₋₂₄ aralkyl, C₇₋₂₄ alkaryl, substituted C₁₋₁₀ alkyl, substituted C₁₋₁₀ alkoxy, substituted C₃₋₁₀ cycloalkyl having 0-3 heteroatoms selected from N, S and O, substituted C₆₋₁₄ aryl, substituted C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from N, S and O, substituted C₇₋₂₄ alkaryl or substituted C₇₋₂₄ aralkyl, where R_y is a substituted group, it is substituted by halogen up to per halo,

R_z is hydrogen, C₁₋₁₀ alkyl, C₁₋₁₀ alkoxy, C₃₋₁₀ cycloalkyl having 0-3 heteroatom, C₂₋₁₀

alkenyl, C₁₋₁₀ alkenoyl, C₆₋₁₂ aryl, C_{3-C12} hetaryl having 1-3 heteroatoms selected from, S, N and O, C₇₋₂₄ alkaryl, C₇₋₂₄ aralkyl, substituted C₁₋₁₀ alkyl, substituted C₁₋₁₀ alkoxy, substituted C_{6-C14} aryl, substituted C_{3-C10} cycloalkyl having 0-3 heteroatoms selected from S, N and O, substituted C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from S, N and O, substituted C₇₋₂₄ alkaryl or substituted C_{7-C24} aralkyl where R_a is a substituted group, it is substituted by halogen up to per halo, hydroxy, C₁₋₁₀ alkyl, C₃₋₁₂ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from N, S and O, C₁₋₁₀ alkoxy, C₆₋₁₂ aryl, C₁₋₆ halo substituted alkyl up to per halo alkyl, C_{6-C12} halo substituted aryl up to per halo aryl, C_{3-C12} halo substituted cycloalkyl up to per halo cycloalkyl having 0-3 heteroatoms selected from N, S and O, halo substituted C_{3-C12} hetaryl up to per halo hetaryl having 1-3 heteroatoms selected from O, N and S, halo substituted C_{7-C24} aralkyl up to per halo aralkyl, halo substituted C_{7-C24} alkaryl up to per halo alkaryl, and -C(O)R_b,

R_a and R_b are,

a) independently hydrogen,

a carbon based moiety selected from the group consisting of C_{1-C10} alkyl, C_{1-C10} alkoxy, C₃₋₁₀ cycloalkyl, C₂₋₁₀ alkenyl, C₁₋₁₀ alkenoyl, C₆₋₁₂ aryl, C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from O, N and S, C₃₋₁₂ cycloalkyl having 0-3 heteroatoms selected from N, S and O, C₇₋₂₄ aralkyl, C_{7-C24} alkaryl, substituted C₁₋₁₀ alkyl, substituted C₁₋₁₀ alkoxy, substituted C₃₋₁₀ cycloalkyl, having 0-3 heteroatoms selected from N, S and O, substituted C₆₋₁₂ aryl, substituted C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from N, S and O, substituted C₇₋₂₄ aralkyl, substituted C₇₋₂₄ alkaryl, where R_a and R_b are a substituted group, they are substituted by halogen up to per halo, hydroxy, C₁₋₁₀ alkyl, C₃₋₁₂ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from N, S and O, C₁₋₁₀ alkoxy, C₆₋₁₂ aryl, C₁₋₆ halo substituted alkyl up to per halo alkyl, C_{6-C12} halo substituted aryl up to per halo aryl, C_{3-C12} halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C_{3-C12} hetaryl up to per halo heteroaryl, halo

substituted C₇-C₂₄ aralkyl up to per halo aralkyl, halo substituted C₇-C₂₄ alkaryl up to per halo alkaryl, and -C(O)R_g; or

-OSi(R_f)₃ where R_f is hydrogen, C₁₋₁₀ alkyl, C₁₋₁₀ alkoxy, C₃₋₁₀ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₆₋₁₂ aryl, C_{3-C12} hetaryl having 1-3 heteroatoms selected from O, S and N, C₇₋₂₄ aralkyl, substituted C₁₋₁₀ alkyl, substituted C_{1-C10} alkoxy, substituted C_{3-C12} cycloalkyl having 0-3 heteroatoms selected from O, S and N, substituted C_{3-C12} heteroaryl having 1-3 heteroatoms selected from O, S, and N, substituted C₆₋₁₂ aryl, and substituted C₇₋₂₄ alkaryl, where R_f is a substituted group it is substituted halogen up to per halo, hydroxy, C₁₋₁₀ alkyl, C₃₋₁₂ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from N, S and O, C₁₋₁₀ alkoxy, C₆₋₁₂ aryl, C_{7-C24} alkaryl, C_{7-C24} aralkyl, C₁₋₆ halo substituted alkyl up to per halo alkyl, C_{6-C12} halo substituted aryl up to per halo aryl, C_{3-C12} halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C_{3-C12} hetaryl up to per halo heteroaryl, halo substituted C_{7-C24} aralkyl up to per halo aralkyl, halo substituted C_{7-C24} alkaryl up to per halo alkaryl, and -C(O)R_g,

or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O with substituents selected from the group consisting of halogen up to per halo, hydroxy, C₁₋₁₀ alkyl, C₃₋₁₂ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from N, S and O, C₁₋₁₀ alkoxy, C₆₋₁₂ aryl, C_{7-C24} alkaryl, C_{7-C24} aralkyl, halo substituted C₁₋₆ alkyl up to per halo alkyl, halo substituted C_{6-C12} aryl up to per halo aryl, halo substituted C_{3-C12} cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C_{3-C12} hetaryl up to per halo heteroaryl, halo substituted C_{7-C24} aralkyl up to per halo aralkyl, halo substituted C_{7-C24} alkaryl up to per halo alkaryl, and -C(O)R_g,

or

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c) one of R_a or R_b is $-C(O)-$, a C_1-C_5 divalent alkylene group or a substituted C_1-C_5 divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_1-C_5 divalent alkylene group are selected from the group consisting of halogen, hydroxy, C_{1-10} alkyl, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{1-10} alkoxy, C_{6-12} aryl, C_7-C_{24} alkaryl, C_7-C_{24} aralkyl, C_{1-6} halo substituted alkyl up to per halo alkyl, C_6-C_{12} halo substituted aryl up to per halo aryl, C_3-C_{12} halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C_3-C_{12} hetaryl up to per halo heteroaryl, halo substituted C_7-C_{24} aralkyl up to per halo aralkyl, halo substituted C_7-C_{24} alkaryl up to per halo alkaryl, and $-C(O)R_g$,

B2 cont

where R_g is C_{1-10} alkyl; $-CN$, $-CO_2R_d$, $-OR_d$, $-SR_d$, $-NO_2$, $-C(O)R_e$, $-NR_dR_e$, $-NR_dC(O)OR_e$ and $-NR_dC(O)R_e$, and R_d and R_e are independently selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{1-10} alkoxy, C_{3-10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, C_{6-12} aryl, C_3-C_{12} hetaryl with 1-3 heteroatoms selected from O, N and S and C_7-C_{24} aralkyl, C_7-C_{24} alkaryl, up to per halo substituted C_1-C_{10} alkyl, up to per halo substituted C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, up to per halo substituted C_6-C_{14} aryl, up to per halo substituted C_3-C_{12} hetaryl having 1-3 heteroatoms selected from O, N, and S, halo substituted C_7-C_{24} alkaryl up to per halo alkaryl, and up to per halo substituted C_7-C_{24} aralkyl,

W is independently selected from the group consisting of $-CN$, $-CO_2R^7$, $-C(O)NR^7R^7$, $-C(O)R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, C_2-C_{10} alkenyl, C_1-C_{10} alkenoyl, C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_6-C_{14} aryl, C_7-C_{24} alkaryl, C_7-C_{24} aralkyl, C_3-C_{12} heteroaryl having 1-3 heteroatoms selected from O, N and S, C_4-C_{23} alkheteroaryl having 1-3 heteroatoms selected from O, N and S, substituted C_1-C_{10} alkyl, substituted C_1-C_{10} alkoxy, substituted C_2-C_{10} alkenyl, substituted C_1-C_{10} alkenoyl, substituted C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from O, N and S,

substituted C₆-C₁₂ aryl, substituted C₃-C₁₂ hetaryl having 1-3 heteroatoms selected from O, N and S, substituted C₇-C₂₄ aralkyl, substituted C₇-C₂₄ alkaryl, substituted C₄-C₂₃ alkheteroaryl having 1-3 heteroatoms selected from O, N and S, and -Q-Ar;

R⁷ is independently selected from H, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₂-C₁₀ alkenyl, C₁-C₁₀ alkenoyl, C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₆-C₁₄ aryl, C₃-C₁₃ hetaryl having 1-3 heteroatoms selected from O, N and S, C₇-C₁₄ alkaryl, C₇-C₂₄ aralkyl, C₄-C₂₃ alkheteroaryl having 1-3 heteroatoms selected from O, N and S, up to per-halosubstituted C₁-C₁₀ alkyl, up to per-halosubstituted C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, N and S, up to per-halosubstituted C₆-C₁₄ aryl, up to per-halosubstituted C₃-C₁₃ hetaryl having 1-3 heteroatoms selected from O, N and S, up to per-halosubstituted C₇-C₂₄ aralkyl, up to per-halosubstituted C₇-C₂₄ alkaryl, and up to per-halosubstituted C₄-C₂₃ alkheteroaryl; and

each Z is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₂-C₁₀ alkenyl, C₁-C₁₀ alkenoyl, C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, N and S, C₆-C₁₄ aryl, C₃-C₁₃ hetaryl having 1-3 heteroatoms selected from O, N and S, C₇-C₂₄ alkaryl, C₇-C₂₄ aralkyl, C₄-C₂₃ alkheteroaryl having 1-3 heteroatoms selected from O, N and S, substituted C₁-C₁₀ alkyl, substituted C₁-C₁₀ alkoxy, substituted C₂-C₁₀ alkenyl, substituted C₁-C₁₀ alkenoyl, substituted C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, N and S, substituted C₆-C₁₂ aryl, substituted C₇-C₂₄ alkaryl, substituted C₇-C₂₄ aralkyl and substituted C₄-C₂₃ alkheteroaryl having 1-3 heteroatoms selected from O, N and S; wherein if Z is a substituted group, the one or more substituents are selected from the group consisting of -CN, -CO₂R⁷, -COR⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NO₂, -NR⁷R⁷, -NR⁷C(O)R⁷, and -NR⁷C(O)OR⁷.

3. (Previously Twice amended) A method as in claim 1 wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m- CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -

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 $N(R^7)(CH_2)_m-$, where $m=1-3$, X^7 is halogen and R^7 is as defined in claim 1.

4. Cancelled

5. Cancelled

46 (Previously Amended) A method of claim 1 wherein B of Formula I is an unsubstituted phenyl group, an unsubstituted pyridyl group, an unsubstituted pyrimidinyl, a phenyl group substituted by a substituent selected from the group consisting of halogen and W_n wherein W and n are as defined in claim 1, a pyrimidinyl group substituted by a substituent selected from the group constituting of halogen and W_n , whereas W and n are as defined in Claim 1, or a substituted pyridyl group substituted by a substituent selected from the group consisting of halogen and W_n wherein W and n are as defined in claim 1.

5 *4*
3 cont *7* (Previously Twice amended) A method of claim *6* wherein B of Formula I is a substituted phenyl group, a substituted pyrimidinyl group, or substituted pyridyl group substituted 1 to 3 times by 1 or more substituents selected from the group consisting of -CN, halogen, C_1-C_{10} alkyl, C_1-C_{10} alkoxy, -OH, up to per halo substituted C_1-C_{10} alkyl, up to per halo substituted C_1-C_{10} alkoxy or phenyl substituted by halogen up to per halo.

6 *8* (Previously Twice amended) A method of claim 1, wherein L, the six member cyclic structure bound directly to D, is a substituted or unsubstituted 6 member aryl moiety or a substituted or unsubstituted 6 member hetaryl moiety, wherein said hetaryl moiety has 1 to 4 members selected from the group of heteroatoms consisting of nitrogen, oxygen and sulfur with the balance of said hetaryl moiety being carbon, wherein the one or more substituents are selected from the group consisting of halogen and W_n wherein W and n are as defined in claim 1.

7 *6*
9 (Previously Twice amended) A method of claim *8*, wherein L, the 6 member cyclic structure bound directly to D, is a substituted phenyl, unsubstituted phenyl, substituted pyrimidinyl, unsubstituted pyrimidinyl, substituted pyridyl or unsubstituted pyridyl group.

8 *10* (Previously Twice amended) A method of claim 1, wherein said substituted cyclic

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moiety L¹ comprises a 5 to 6 membered aryl moiety or heteraryl moiety, wherein said heteraryl moiety comprises 1 to 4 members selected from the group of heteroatoms consisting of nitrogen, oxygen and sulfur.

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11. (Previously Twice amended) A method of claim 2, wherein said substituted cyclic moiety L¹ is phenyl, pyridinyl or pyrimidinyl.

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12. (Previously Twice amended) A method of claim 3, wherein said substituted cyclic moiety L¹ is phenyl, pyridinyl or pyrimidinyl.

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13. (Currently thrice amended) A method of claim 8 ⁴ 8, wherein said substituted cyclic moiety L¹ is phenyl, pyridinyl or pyrimidinyl.

14. Cancelled

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15. (Currently thrice amended) A method of claim 8 ⁵ 7, wherein said substituted cyclic moiety L¹ is phenyl, pyridinyl or pyrimidinyl.

16. Cancelled

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17. (Currently thrice amended) A method of claim 8 ⁶ 10, wherein said substituted cyclic moiety L¹ is phenyl, pyridinyl or pyrimidinyl.

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18. (Currently thrice amended) A method of claim 13 ¹¹ 17, wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m-CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, X^a is halogen and R⁷ is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.

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19. (Previously Twice amended) A method of claim 15 ¹² 18, wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m-CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, X^a is halogen and R⁷ is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.

20. Cancelled

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¹⁶ 21. (Previously Twice amended) A method of claim ¹³ 17, wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m-CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, X^a is halogen and R⁷ is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.

22. Cancelled

23. Cancelled

24. Cancelled

25. Cancelled

26. Cancelled

B2 cont
¹⁸ 27. (Previously Twice amended) A method of claim ¹⁶ 21 wherein L¹ is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of C₁-C₁₀ alkyl, up to per halo substituted C₁-C₁₀ alkyl, -CN, -OH, halogen, C₁-C₁₀ alkoxy and up to per halo substituted C₁-C₁₀ alkoxy.

¹⁹ 28. (Previously Twice amended) A method of claim 1 wherein L¹ is substituted by -C(O)R_x.

29. Cancelled

30. Cancelled

31. Cancelled

²⁰ 32. (Currently thrice amended) A method of claim 1 wherein L¹ is pyridinyl substituted by -C(O)R_x or -SO₂R_x, wherein R_x is NR_aR_b.

²¹ 33. (Previously Twice amended) A method of claim ¹¹ 32 wherein L¹ is pyridinyl substituted by -C(O)R_x or -SO₂R_x, wherein R_x is NR_aR_b, and R_a and R_b are

a) independently hydrogen,

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a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

-OSi(R_f)₃ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

B² cont
c) one of R_a or R_b is -C(O)-, a C₁-C₅ divalent alkylene group or a substituted C₁-C₅ divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C₁-C₅ divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.

34. Cancelled

35. Cancelled

36. Cancelled

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37. (Previously Twice amended) A method of claim 21 wherein L¹ is substituted by -C(O)R_x or -SO₂R_x, wherein R_x is NR_aR_b and R_a and R_b are independently hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally

substituted by halogen.

38. (Previously Twice amended) A method for the treatment of cancerous cell growth mediated by RAF kinase, comprising administering a compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is $-NH-C(O)-NH-$,

A is a substituted moiety of up to 40 carbon atoms of the formula: $-L-(M-L^1)_q$, where L is a 6 membered aryl moiety or a 6 membered hetaryl moiety bound directly to D, L^1 comprises a substituted cyclic moiety having at least 5 members, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and L^1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur,

wherein L^1 is substituted by at least one substituent selected from the group consisting of $-SO_2R_x$, $-C(O)R_x$ and $-C(NR_y)R_z$,

R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo,

R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

R_x is R_z or NR_aR_b where R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and

but C1
carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

-OSi(R₂)₃ where R₂ is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R₄ and R₅ together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

B2 cont
c) one of R₄ or R₅ is -C(O)-, a C₁-C₃ divalent alkylene group or a substituted C₁-C₃ divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C₁-C₃ divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L¹ is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and W_n, where n is 0-3;

wherein each W is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)NR⁷R⁷, -C(O)-R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, -Q-Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NR⁷R⁷, -NO₂, -NR⁷C(O)R⁷, -NR⁷C(O)OR⁷ and halogen up to per-halo; with each R⁷ independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

sub C1
wherein Q is -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-,
-(CH₂)_mN(R⁷)-, -O(CH₂)_m- CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, and X^a
is halogen;

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the
group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to
per-halo, and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently
selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -NO₂, -OR⁷, -SR⁷, -
NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, and a carbon based moiety of up to 24 carbon atoms,
optionally containing heteroatoms selected from N, S and O and optionally substituted by one
or more substituents are selected from the group consisting of -CN, -CO₂R⁷, -COR⁷, -
C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NO₂, -NR⁷R⁷, -NR⁷C(O)R⁷, and -NR⁷C(O)OR⁷, with R⁷ as defined
above; and

Bent
wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R⁷)-
, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m- CHX^a-, -CX^a₂-,
-S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, X^a is halogen.

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39. (Currently thrice amended) A method for the treatment of cancerous cell growth
mediated by RAF kinase, comprising administering a compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is a substituted moiety of up to 40 carbon atoms of the formula: -L-(M-L¹)_q, where
L is a substituted or unsubstituted phenyl or pyridinyl moiety bound directly to D, L¹ comprises
a substituted phenyl, pyridinyl or pyrimidinyl moiety, M is a bridging group having at least one
atom, q is an integer of from 1-3; and

B is a substituted or unsubstituted phenyl or pyridine group bound directly to D,

wherein L¹ is substituted by at least one substituent selected from the group consisting of
-SO₂R_x, -C(O)R_x and -C(NR_y)R_z,

part C.1
 R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo, and ;

R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

R_x is R_z or NR_aR_b where R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

Bent
-OSi(R_f)₃ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R_a or R_b is -C(O)-, a C₁-C₃ divalent alkylene group or a substituted C₁-C₃ divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C₁-C₃ divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

Sub C1
where B is substituted, L is substituted or L¹ is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and W_n, where n is 0-3;

wherein each W is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)NR⁷R⁷, -C(O)-R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, -Q-Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NR⁷R⁷, -NO₂, -NR⁷C(O)R⁷, -NR⁷C(O)OR⁷ and halogen up to per-halo; with each R⁷ independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m-CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, and X^a is halogen;

B2 cont
Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of -CN, -CO₂R⁷, -COR⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NO₂, -NR⁷R⁷, -NR⁷C(O)R⁷, and -NR⁷C(O)OR⁷; and

wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m-CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, X^a is halogen.

40. Cancelled
41. Cancelled
42. Cancelled

25
44
23. (Previously Twice amended) A method as in claim 38 wherein substituents for B and L and additional substituents for L¹, are selected from the group consisting of C₁-C₁₀ alkyl up to per halo substituted C₁-C₁₀ alkyl, CN, OH, halogen, C₁-C₁₀ alkoxy and up to per halo substituted C₁-C₁₀ alkoxy.

26
25. (Previously Twice amended) A method as in claim 39 wherein substituents for B and L and additional substituents for L¹, are selected from the group consisting of C₁-C₁₀ alkyl up to per halo substituted C₁-C₁₀ alkyl, CN, OH, halogen, C₁-C₁₀ alkoxy and up to per halo substituted C₁-C₁₀ alkoxy.

27
26. (Currently thrice amended) A method of claim 38 wherein L¹ is pyridinyl substituted by C(O)R_x or SO₂R_x.

28
47. (Currently thrice amended) A method of claim 39 wherein L¹ is pyridinyl substituted by C(O)R_x or SO₂R_x.

29
48. (Previously Twice amended) A method of claim 46 wherein R_x is NR_aR_b and R_a and R_b are independently hydrogen and a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen..

30
49. (Previously Twice Amended) A method of claim 47 wherein R_x is NR_aR_b and R_a and R_b are independently hydrogen and a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.

31
50. (Previously Twice amended) A method of claim 1 wherein the compound of formula 1 is a pharmaceutically acceptable salt selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid

for C1
(tosylate salt), 1-napthalene sulfonic acid, 2-napthalene/sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

51. Cancelled

32

21
52. (Previously Twice amended) A method of claim 33 wherein the compound of formula 1 is a pharmaceutically acceptable salt selected from the group consisting of

Bent
a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

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23
53. (Previously Twice amended) A method of claim 38 wherein the compound of formula 1 is a pharmaceutically acceptable salt selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

Sub C17
b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

³⁴
54. (Previously Twice amended) A method of claim ³⁴39 wherein the compound of formula 1 is a pharmaceutically acceptable salt selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

55. Cancelled

56. Cancelled

57. Cancelled

58. Cancelled

59. Cancelled

60. Cancelled

61. Cancelled

62. Cancelled

63. Cancelled

64. Cancelled

65. Cancelled

³⁵
66. (Currently twice amended) A method for the treatment of a cancerous cell growth

mediated by raf kinase, comprising ~~administering~~ administering a compound selected from the group consisting of

3-tert butyl phenyl ureas of Table 1 above;

5-tert butyl-2-methoxyphenyl ureas of Table 2 above;

5-(trifluoromethyl)-2 phenyl ureas of Table 3 above;

3-(trifluoromethyl)-4 chlorophenyl ureas of Table 4 above;

3-(trifluoromethyl)-4-bromophenyl ureas of Table 5 above;

5-(trifluoromethyl)-4-chloro-2 methoxyphenyl ureas of Table 6 above; and

ureas 101-103 in Table 7 above.

^{3le}
57. (Currently Twice amended) A method for the treatment of a cancerous cell growth mediated by raf kinase, comprising ~~administering~~ administering a compound selected from the group consisting of

the 3-tert butyl phenyl ureas:

N-(3-tert-butylphenyl)-*N'*-(4-(3-(*N*-methylcarbamoyl)phenoxy)phenyl) urea and

N-(3-tert-butylphenyl)-*N'*-(4-(4-acetylphenoxy)phenyl) urea;

the 5-tert-butyl-2-methoxyphenyl ureas:

N-(5-tert-butyl-2-methoxyphenyl)-*N'*-(4-(1,3-dioxoisindolin-5-yloxy)phenyl) urea,

N-(5-tert-butyl-2-methoxyphenyl)-*N'*-(4-(1-oxoisindolin-5-yloxy)phenyl) urea,

N-(5-tert-butyl-2-methoxyphenyl)-*N'*-(4-(4-methoxy-3-(*N*-methylcarbamoyl)phenoxy)phenyl) urea

and

N-(5-tert-butyl-2-methoxyphenyl)-*N'*-(4-(3-(*N*-methylcarbamoyl)phenoxy)phenyl) urea;

the 2-methoxy-5-trifluoromethylphenyl ureas:

N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(3-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

Part C1
N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(3-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,
N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,
N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,
N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridylthio)phenyl) urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(2-chloro-4-(2-(*N*-methylcarbamoyl)(4-pyridyloxy))phenyl) urea and

N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(3-chloro-4-(2-(*N*-methylcarbamoyl)(4-pyridyloxy))phenyl) urea;

the 4-chloro-3-(trifluoromethyl)phenyl ureas:

B2 cont
N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(3-(2-carbamoyl-4-pyridyloxy)phenyl) urea,
N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(3-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,
N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea and
N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea;

the 4-bromo-3-(trifluoromethyl)phenyl ureas:

N-(4-bromo-3-(trifluoromethyl)phenyl)-*N'*-(3-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,
N-(4-bromo-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,
N-(4-bromo-3-(trifluoromethyl)phenyl)-*N'*-(3-(2-(*N*-methylcarbamoyl)-4-pyridylthio)phenyl) urea,
N-(4-bromo-3-(trifluoromethyl)phenyl)-*N'*-(2-chloro-4-(2-(*N*-methylcarbamoyl)(4-pyridyloxy))phenyl) urea and
N-(4-bromo-3-(trifluoromethyl)phenyl)-*N'*-(3-chloro-4-(2-(*N*-methylcarbamoyl)(4-pyridyloxy))phenyl) urea; and

the 2-methoxy-4-chloro-5-(trifluoromethyl)phenyl ureas:

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N'*-(3-(2-(*N*-methylcarbamoyl)-4-

pyridyloxy)phenyl) urea,

Sub C1
67
68. ~~N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,~~

~~N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea and~~

~~N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(3-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea.~~

67
68. (Currently twice amended) A method ~~as in claim 1~~ for the treatment of solid cancers mediated by raf kinase in a human comprising administering a compound of Formula I:

A - D - B _____ (I)

B² cent
or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-

A is a substituted moiety of up to 40 carbon atoms of the formula: -L-(M-L¹)_q, where L is a 5 or 6 membered cyclic structure bound directly to D, L¹ comprises a substituted cyclic moiety having at least 5 members, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and L¹ contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur,

wherein L¹ is substituted by at least one substituent selected from the group consisting of -SO₂R_x, -C(O)R_y and -C(NR_y) R_z,

R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo,

R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing

ph
C1

heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

R_x is R_z or NR_eR_b where R_e and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

-OSi(R_f); where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

B² cent

b) R_e and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R_e or R_b is -C(O)-, a C_1 - C_3 divalent alkylene group or a substituted C_1 - C_3 divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_1 - C_3 divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L^1 is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and W_n , where n is 0-3;

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C1
wherein each W is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)NR⁷R⁷, -C(O)-R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, -O-Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NR⁷R⁷, -NO₂, -NR⁷C(O)R⁷, -NR⁷C(O)OR⁷ and halogen up to per-halo; with each R⁷ independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen.

wherein Q is -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m-CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, and X^a is halogen; and

B2 cont
Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of -CN, -CO₂R⁷, -COR⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NO₂, -NR⁷R⁷, -NR⁷C(O)R⁷, and -NR⁷C(O)OR⁷, with R⁷ as defined above.

38
69. (Currently amended) A method ~~as in claim 1~~ for the treatment of carcinomas, myleoid disorders or adenomas in a human mediated by RAF kinase comprising administering a compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-

pub
C1

A is a substituted moiety of up to 40 carbon atoms of the formula: $-L-(M-L^1)_q$, where L is a 5 or 6 membered cyclic structure bound directly to D, L^1 comprises a substituted cyclic moiety having at least 5 members, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and L^1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur,

wherein L^1 is substituted by at least one substituent selected from the group consisting of $-SO_2R_x$, $-C(O)R_x$ and $-C(NR_y)R_z$,

R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo,

B2 cont
 R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

R_x is R_z or NR_aR_b where R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

$-OSi(R_f)_3$ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally

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contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R_a or R_b is -C(O)-, a C₁-C₅ divalent alkylene group or a substituted C₁-C₅ divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C₁-C₅ divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

B2 cont
where B is substituted, L is substituted or L¹ is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and W_n, where n is 0-3;

wherein each W is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)NR⁷R⁷, -C(O)R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, -O-Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NR⁷R⁷, -NO₂, -NR⁷C(O)R⁷, -NR⁷C(O)OR⁷ and halogen up to per-halo; with each R⁷ independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein O is -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m-, -CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, where m= 1-3, and X^a is halogen; and

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the

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group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1} , wherein $n1$ is 0 to 3 and each Z is independently selected from the group consisting of $-CN$, $-CO_2R^7$, $-C(O)R^7$, $-C(O)NR^7R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of $-CN$, $-CO_2R^7$, $-COR^7$, $-C(O)NR^7R^7$, $-OR^7$, $-SR^7$, $-NO_2$, $-NR^7R^7$, $-NR^7C(O)OR^7$, and $-NR^7C(O)R^7$, with R^7 as defined above.

- 39*
39. (Currently twice amended) A method as in claim 28 *23* 38 for the treatment of carcinomas, myleoid disorders or adenomas.
- 40*
40. (Previously amended) A method as in claim *24* 39 for the treatment of carcinomas, myleoid disorders or adenomas.
- 41*
41. (Previously amended) A method as in claim *31* 50 for the treatment of carcinomas, myleoid disorders or adenomas.
- 42*
42. (Previously amended) A method as in claim *36* 67 for the treatment of carcinomas, myleoid disorders or adenomas.
- 43*
43. (Previously amended) A method as in claim 1 for the treatment of carcinoma of the lung, pancreas, thyroid, bladder or colon mediated by RAF kinase.
- 44*
44. (Currently twice amended) A method as in claim 28 *23* 38 for the treatment of carcinoma of the lung, pancreas, thyroid, bladder or colon.
- 45*
45. (Previously amended) A method as in claim *24* 39 for the treatment of carcinoma of the lung, pancreas, thyroid, bladder or colon.
- 46*
46. (Previously amended) A method as in claim *31* 50 for the treatment of carcinoma of the lung, pancreas, thyroid, bladder or colon.
- 47*
47. (Previously amended) A method as in claim *36* 67 for the treatment of carcinoma of the lung, pancreas, thyroid, bladder or colon.

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⁴⁸
79. (Previously amended) A method as in claim 1 for the treatment of myeloid leukemia or villous colon adenomas mediated by RAF kinase.

⁴⁹
80. (Previously amended) A method as in claim ¹⁹28 for the treatment of myeloid leukemia or villous colon adenomas.

⁵⁰
81. (Previously amended) A method as in claim ²⁴39 for the treatment of myeloid leukemia or villous colon adenomas.

B2 cont
⁵¹
82. (Previously amended) A method as in claim ³50 for the treatment of myeloid leukemia or villous colon adenomas.

⁵²
83. (Previously amended) A method as in claim ³⁶61 for the treatment of myeloid leukemia or villous colon adenomas.